SHORT COMMUNICATION

An Approach for the Analysis of the Development of Tumors under the Influence of Various Factors

E.L. Pankratov
[1]Nizhny Novgorod State University, 23 Gagarin Avenue, Nizhny Novgorod, 603950, Russia
[2]Nizhny Novgorod State Agrotechnological University, 97 Gagarin Avenue, Nizhny Novgorod, 603950, Russia

ABSTRACT: We introduce a model to describe tumor development. The model takes into account the development of their own cells, the effects of chemotherapeutic drugs on them, as well as their interaction with surrounding cells. We also introduce an analytical approach for the analysis of the introduced model. The approach gives the possibility to take into account changes in the conditions of the processes considered: changes in the properties of tissues in space and time, as well as the nonlinearity of the development of tumors. We analyzed the possibility of accelerating and decelerating the development of the tumor depending on the parameters of the considered process. The possibility of changing their rates is being considered.

KEYWORDS: model of tumor development; changing of rate of development of tumor; analytical approach for analysis.

https://doi.org/10.29294/IJASE.10.2.2023.3355-3361

INTRODUCTION

The development of cancerous tumors is associated with various chemical, genetic, physiological, and mechanical factors that occur both at the subcellular and cellular levels, as well as at the levels of tissues and organs. In recent decades, one can find progress in identifying and explaining the processes that occur during the development of cancer, as well as developing methods and tools for early diagnosis and treatment of the disease [1-7]. The development of biotechnologies and medicine has allowed us to lay significant groundwork for the treatment of the disease in question. A significant part of the study of tumor development is its prognosis based on experimental data and mathematical models. We introduce a model of tumor development. The model gives them the possibility of taking into account the development of their own cells, the effects of chemotherapeutic drugs on them, as well as their interaction with surrounding cells. We also introduce an analytical approach for the analysis of the introduced model. The model gives the possibility of taking into account changes in the conditions of the considered processes. We also consider the possibility of changing their flow rate.
Method of solution

In this section, we consider a model to estimate the development of tumors, their own growth, the influence of chemotherapeutic drugs on the above cells, as well as their interaction with surrounding cells. We determine the required spatio-temporal distribution of the number of the considered cells as the solution of the second Fick's law in the following form:

$$\frac{\partial N(x,y,z,t)}{\partial t}=\frac{\partial}{\partial x}\left[D(x,y,z,T)\frac{\partial N(x,y,z,t)}{\partial x}\right]+\frac{\partial}{\partial y}\left[D(x,y,z,T)\frac{\partial N(x,y,z,t)}{\partial y}\right]$$
$$+\frac{\partial}{\partial z}\left[D(x,y,z,T)\frac{\partial N(x,y,z,t)}{\partial z}\right]+\frac{R_1(x,y,z,t)N(x,y,z,t)}{1+R_2(x,y,z,t)N^2(x,y,z,t)}-C(x,y,z,t)$$
$$-\frac{A_1(x,y,z,t)N(x,y,z,t)}{1+A_2(x,y,z,t)N^2(x,y,z,t)}-M(x,y,z,t)\,N(x,y,z,t), \qquad (1)$$

where $N(x,y,z,t)$ is the quantity of tumor cells; terms with functions $R_i(x,y,z,t)$ describes the rate of division of tumor cells; terms with function $M(x,y,z,t)$ describes the rate of natural mortality of tumor cells; the term with the functions $A_i(x,y,z,t)$ describes the rate of death of tumor cells due to their bioavailability to an active chemotherapeutic drug; $S(x,y,z,t)$ is the rate of death of tumor cells due to

***Corresponding Author: elp2004@mail.ru**
Received: 08.09.2023 **Accepted:** 17.10.2023 **Published on**: 25.11.2023

competition with surrounding cells; D (x,y,z,t) is the cell diffusion coefficient; x, y and z are the spatial coordinates; t is the time; T is the temperature. The initial distribution of tumor cells and the boundary conditions for equation (1) are represented in the following form

$$-D(x,y,z,t)\frac{\partial N(x,y,z,t)}{\partial x}\bigg|_{x=0}=J_{x1},\ -D(x,y,z,t)\frac{\partial N(x,y,z,t)}{\partial x}\bigg|_{x=L_x}=J_{x2},\ (2)$$

$$-D(x,y,z,t)\frac{\partial N(x,y,z,t)}{\partial y}\bigg|_{y=0}=J_{y1},\ -D(x,y,z,t)\frac{\partial N(x,y,z,t)}{\partial y}\bigg|_{y=L_y}=J_{y2},$$

$$-D(x,y,z,t)\frac{\partial N(x,y,z,t)}{\partial z}\bigg|_{z=0}=J_{z1},\ -D(x,y,z,t)\frac{\partial N(x,y,z,t)}{\partial z}\bigg|_{z=L_z}=J_{z2},$$

$$N(x,y,z,0)=f(x,y,z).$$

We determine the solutions of equation (1) using the method of averaging functional corrections [8-11]. In the framework of the method, we will substitute in the right parts of equations (1) the not yet known average value of the desired number of cells α_1 instead of the function N (x,y,z,t), i.e. we use the following replacement N $(x,y,z,t)\to\alpha_1$. Then we obtain the following equation to determine the first-order approximation of the number of tumor cells in the following form:

$$\frac{d\,N_1(x,y,z,t)}{d\,t}=\frac{R_1(x,y,z,t)\,\alpha_1}{1+R_2(x,y,z,t)\,\alpha_1^2}-\frac{A_1(x,y,z,t)\,\alpha_1}{1+A_2(x,y,z,t)\,\alpha_1^2}-$$
$$-M(x,y,z,t)\,\alpha_1-C(x,y,z,t).\ (3)$$

Integration of the right and the left sides of equation (3) on time gives a possibility to obtain a ratio for the first-order approximation of the number of the considered cells $N_1(x,y,z,t)$ in the final form

$$N_1(x,y,z,t)=\alpha_1\int_0^t\frac{R_1(x,y,z,\tau)\,d\tau}{1+R_2(x,y,z,\tau)\,\alpha_1^2}-\alpha_1\int_0^t M(x,y,z,\tau)\,d\tau-\alpha_1\int_0^t\frac{A_1(x,y,z,\tau)\,d\tau}{1+A_2(x,y,z,\tau)\,\alpha_1^2}$$
$$-\int_0^t C(x,y,z,\tau)\,d\tau+f(x,y,z).\qquad(4)$$

The not yet known average value α_1 was calculated by using the following standard relation [8-10]

$$\alpha_1=\frac{1}{L_xL_yL_z\Theta}\int_0^\Theta\int_0^{L_x}\int_0^{L_y}\int_0^{L_z}N_1(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t.\qquad(5)$$

Substitution of relation (4) into relation (5) gives a possibility to obtain the following equation to determine the above average value

$$\alpha_1\int_0^\Theta(\Theta-t)\int_0^{L_x}\int_0^{L_y}\int_0^{L_z}\left[\frac{R_1(x,y,z,t)}{1+R_2(x,y,z,t)\,\alpha_1^2}+\frac{A_1(x,y,z,t)}{1+A_2(x,y,z,t)\,\alpha_1^2}\right]d\,z\,d\,y\,d\,x\,d\,t+\alpha_1\Big[L_xL_yL_z\Theta-$$
$$\int_0^\Theta(\Theta-t)\int_0^{L_x}\int_0^{L_y}\int_0^{L_z}M(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t\Big]-\int_0^\Theta(\Theta-t)\int_0^{L_x}\int_0^{L_y}\int_0^{L_z}C(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t+$$
$$\int_0^\Theta\int_0^{L_x}\int_0^{L_y}\int_0^{L_z}f(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t=0.\qquad(6)$$

Solution of equation (6) could be written as

$$\alpha_1=\Bigg\{\int_0^\Theta(\Theta-t)\int_0^{L_x}\int_0^{L_y}\int_0^{L_z}C(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t-\int_0^\Theta\int_0^{L_x}\int_0^{L_y}\int_0^{L_z}f(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t-L_xL_yL_z\Theta+$$

$$\int_0^\Theta (\Theta-t)\int_0^{L_x}\int_0^{L_y}\int_0^{L_z} M(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t-\int_0^\Theta (\Theta-t)\int_0^{L_x}\int_0^{L_y}\int_0^{L_z} R_1(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t-L_xL_yL_z\Theta\times$$
$$\int_0^\Theta (\Theta-t)\int_0^{L_x}\int_0^{L_y}\int_0^{L_z} A_2(x,y,z,t)M(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t+\int_0^\Theta (\Theta-t)\int_0^{L_x}\int_0^{L_y}\int_0^{L_z} A_2(x,y,z,t)\times$$
$$M(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t-\int_0^\Theta (\Theta-t)\int_0^{L_x}\int_0^{L_y}\int_0^{L_z} A_2(x,y,z,t)\,f(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t-$$
$$\int_0^\Theta (\Theta-t)\int_0^{L_x}\int_0^{L_y}\int_0^{L_z}\left[A_2(x,y,z,t)R_1(x,y,z,t)+A_1(x,y,z,t)R_2(x,y,z,t)\right]d\,z\,d\,y\,d\,x\,d\,t+$$
$$\int_0^\Theta (\Theta-t)\int_0^{L_x}\int_0^{L_y}\int_0^{L_z} A_2(x,y,z,t)\,R_2(x,y,z,t)\left[M(x,y,z,t)-f(x,y,z,t)\right]d\,z\,d\,y\,d\,x\,d\,t-$$
$$\int_0^\Theta (\Theta-t)\int_0^{L_x}\int_0^{L_y}\int_0^{L_z} R_2(x,y,z,t)\,f(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t-\int_0^\Theta (\Theta-t)\int_0^{L_x}\int_0^{L_y}\int_0^{L_z} A_2(x,y,z,t)\times$$
$$f(x,y,z,t)R_2(x,y,z,t)d\,z\,d\,y\,d\,x\,d\,t-L_xL_yL_z\Theta\int_0^\Theta (\Theta-t)\int_0^{L_x}\int_0^{L_y}\int_0^{L_z} A_2(x,y,z,t)\times$$
$$R_2(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t\ \Big\}^{1/2}. \tag{6}$$

The second-order approximation of the required quantity of tumor cells in the framework of the method of averaging function corrections could be obtained by using the following standard replacement: $N(x,y,z,t)\rightarrow \alpha_2+N_1(x,y,z,t)$ in the right side of equation (1) [8-11]. The substitution gives a possibility to obtain the following equation to calculate the considered approximation

$$\frac{\partial N_2(x,y,z,t)}{\partial t}=\frac{\partial}{\partial x}\left[D(x,y,z,T)\frac{\partial N_1(x,y,z,t)}{\partial x}\right]+\frac{\partial}{\partial y}\left[D(x,y,z,T)\frac{\partial N_1(x,y,z,t)}{\partial y}\right]+$$
$$\frac{\partial}{\partial z}\left[D(x,y,z,T)\frac{\partial N(x,y,z,t)}{\partial z}\right]+\frac{R_1(x,y,z,t)\left[\alpha_2+N_1(x,y,z,t)\right]}{1+R_2(x,y,z,t)\left[\alpha_2+N_1(x,y,z,t)\right]^2}-C(x,y,z,t)-$$
$$\frac{A_1(x,y,z,t)\left[\alpha_2+N_1(x,y,z,t)\right]}{1+A_2(x,y,z,t)\left[\alpha_2+N_1(x,y,z,t)\right]^2}-M(x,y,z,t)\left[\alpha_2+N_1(x,y,z,t)\right]. \tag{7}$$

Integration of right and left sides of equation (7) on time gives a possibility to obtain the following relation to calculate the second-order approximation of the considered cells $N_2(x,y,z,t)$ in the following final form:

$$N_2(x,y,z,t)=\frac{\partial}{\partial x}\int_0^t D(x,y,z,T)\frac{\partial N_1(x,y,z,\tau)}{\partial x}d\,\tau+\frac{\partial}{\partial y}\int_0^t D(x,y,z,T)\frac{\partial N_1(x,y,z,\tau)}{\partial y}d\,\tau+$$
$$\frac{\partial}{\partial z}\int_0^t D(x,y,z,T)\frac{\partial N_1(x,y,z,\tau)}{\partial z}d\,\tau+\int_0^t\frac{R_1(x,y,z,\tau)\left[\alpha_2+N_1(x,y,z,\tau)\right]d\,\tau}{1+R_2(x,y,z,\tau)\left[\alpha_2+N_1(x,y,z,\tau)\right]^2}-$$
$$\int_0^t\frac{A_1(x,y,z,\tau)\left[\alpha_2+N_1(x,y,z,\tau)\right]d\,\tau}{1+A_2(x,y,z,\tau)\left[\alpha_2+N_1(x,y,z,\tau)\right]^2}-\int_0^t M(x,y,z,\tau)\left[\alpha_2+N_1(x,y,z,\tau)\right]d\,\tau-$$
$$\int_0^t C(x,y,z,\tau)\,d\,\tau+f(x,y,z). \tag{8}$$

Average value of the second-order approximation of the considered quantity of sells α_2 could be calculated by using the following standard relation [8-11]

Pankratov

$$\alpha_2 = \frac{1}{L_x L_y L_z \Theta}\int\limits_0^{\Theta}\int\limits_0^{L_x}\int\limits_0^{L_y}\int\limits_0^{L_z}\left[N_2(x,y,z,t)-N_1(x,y,z,t)\right]d\,z\,d\,y\,d\,x\,d\,t. \quad (9)$$

Substitution of relations (4) and (8) into relation (9) gives a possibility to obtain the following equation to determine the not yet known average value α_2

$$\int\limits_0^{\Theta}(\Theta-t)\int\limits_0^{L_x}\int\limits_0^{L_y}\int\limits_0^{L_z}\frac{R_1(x,y,z,t)\left[\alpha_2+N_1(x,y,z,t)\right]d\,z}{1+R_2(x,y,z,\tau)\left[\alpha_2+N_1(x,y,z,\tau)\right]^2}\,d\,y\,d\,x\,d\,t-\alpha_2\left[L_xL_yL_z\Theta+\int\limits_0^{\Theta}(\Theta-t)\times\right.$$

$$\left.\int\limits_0^{L_x}\int\limits_0^{L_y}\int\limits_0^{L_z}M(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t\right]-\int\limits_0^{\Theta}\int\limits_0^{L_x}\int\limits_0^{L_y}\int\limits_0^{L_z}\frac{A_1(x,y,z,t)\left[\alpha_2+N_1(x,y,z,t)\right]d\,z}{1+A_2(x,y,z,t)\left[\alpha_2+N_1(x,y,z,t)\right]^2}\,d\,y\,d\,x\,\times$$

$$(\Theta-t)\,d\,t+\int\limits_0^{\Theta}(\Theta-t)\int\limits_0^{L_x}\int\limits_0^{L_y}\int\limits_0^{L_z}\left[\frac{\alpha_1 A_1(x,y,z,t)}{1+A_2(x,y,z,t)\,\alpha_1^2}-\frac{\alpha_1 R_1(x,y,z,t)}{1+R_2(x,y,z,t)\,\alpha_1^2}\right]d\,z\,d\,y\,d\,x\,d\,t-$$

$$\int\limits_0^{\Theta}(\Theta-t)\int\limits_0^{L_x}\int\limits_0^{L_y}\int\limits_0^{L_z}C(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t+\alpha_1\int\limits_0^{\Theta}(\Theta-t)\int\limits_0^{L_x}\int\limits_0^{L_y}\int\limits_0^{L_z}M(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t-$$

$$\int\limits_0^{\Theta}(\Theta-t)\int\limits_0^{L_x}\int\limits_0^{L_y}\int\limits_0^{L_z}N_1(x,y,z,t)M(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t+\int\limits_0^{\Theta}\int\limits_0^{L_y}\int\limits_0^{L_z}\left[J_{2x}(y,z,t)-J_{1x}(y,z,t)\right]d\,z\,d\,y\,\times$$

$$(\Theta-t)\,d\,t+\int\limits_0^{\Theta}(\Theta-t)\int\limits_0^{L_y}\int\limits_0^{L_z}\left[J_{2y}(y,z,t)-J_{1y}(y,z,t)\right]d\,z\,d\,y\,d\,t+\int\limits_0^{\Theta}(\Theta-t)\int\limits_0^{L_x}\int\limits_0^{L_y}\left[J_{2z}(y,z,t)-\right.$$

$$\left.J_{1z}(y,z,t)\right]d\,y\,d\,x\,d\,t+\int\limits_0^{\Theta}(\Theta-t)\int\limits_0^{L_x}\int\limits_0^{L_y}\int\limits_0^{L_z}C(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t=0. \quad (10)$$

Solution of equation (10) could be presented in the following form

$$\alpha_2=\int\limits_0^{\Theta}(\Theta-t)\int\limits_0^{L_x}\int\limits_0^{L_y}\int\limits_0^{L_z}A_1(x,y,z,t)N_1(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t-\int\limits_0^{\Theta}\int\limits_0^{L_x}\int\limits_0^{L_y}\int\limits_0^{L_z}C(x,y,z,t)\,d\,z\,d\,y\,d\,x\,\times$$

$$(\Theta-t)\,d\,t-\int\limits_0^{\Theta}(\Theta-t)\int\limits_0^{L_x}\int\limits_0^{L_y}\int\limits_0^{L_z}\left[A_2(x,y,z,t)+R_2(x,y,z,t)\right]N_1^2(x,y,z,t)\times$$

$$C(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t-\int\limits_0^{\Theta}(\Theta-t)\int\limits_0^{L_x}\int\limits_0^{L_y}\int\limits_0^{L_z}R_1(x,y,z,t)N_1(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t+$$

$$\int\limits_0^{\Theta}\int\limits_0^{L_x}\int\limits_0^{L_y}\int\limits_0^{L_z}N_1^3(x,y,z,t)\left[A_1(x,y,z,t)R_2(x,y,z,t)-A_2(x,y,z,t)R_1(x,y,z,t)\right]d\,z\,d\,y\,d\,x\,\times$$

$$(\Theta-t)\,d\,t-\int\limits_0^{\Theta}(\Theta-t)\int\limits_0^{L_x}\int\limits_0^{L_y}\int\limits_0^{L_z}A_2(x,y,z,t)N_1^4(x,y,z,t)C(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t+$$

$$\int\limits_0^{\Theta}(\Theta-t)\int\limits_0^{L_x}\int\limits_0^{L_y}\int\limits_0^{L_z}A_1(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t+\int\limits_0^{\Theta}(\Theta-t)\int\limits_0^{L_x}\int\limits_0^{L_y}\int\limits_0^{L_z}M(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t+$$

$$L_xL_yL_z\Theta-2\int\limits_0^{\Theta}(\Theta-t)\int\limits_0^{L_x}\int\limits_0^{L_y}\int\limits_0^{L_z}A_2(x,y,z,t)C(x,y,z,t)N_1(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t-$$

$$\int\limits_0^{\Theta}(\Theta-t)\int\limits_0^{L_x}\int\limits_0^{L_y}\int\limits_0^{L_z}R_1(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t+\int\limits_0^{\Theta}\int\limits_0^{L_x}\int\limits_0^{L_y}\int\limits_0^{L_z}A_2(x,y,z,t)N_1^2(x,y,z,t)\,d\,z\,d\,y\,d\,x\,\times$$

$$
\begin{aligned}
&(\Theta-t)\,d\,t\left[L_xL_yL_z\Theta+\int_0^\Theta(\Theta-t)\int_0^{L_x}\int_0^{L_y}\int_0^{L_z}M(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t\right]+3\int_0^\Theta\int_0^{L_x}\int_0^{L_y}\int_0^{L_z}[A_1(x,y,z,t)\times\\
&R_2(x,y,z,t)-A_2(x,y,z,t)R_1(x,y,z,t)]N_1^2(x,y,z,t)\,d\,z\,d\,y\,d\,x(\Theta-t)\,d\,t- \qquad (11)\\
&2\int_0^\Theta(\Theta-t)\int_0^{L_x}\int_0^{L_y}\int_0^{L_z}C(x,y,z,t)N_2(x,y,z,t)\,R_2(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t+\int_0^\Theta(\Theta-t)\times\\
&\int_0^{L_x}\int_0^{L_y}\int_0^{L_z}R_2(x,y,z,t)N_1^2(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t\left[\int_0^\Theta(\Theta-t)\int_0^{L_x}\int_0^{L_y}\int_0^{L_z}M(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t+\right.\\
&\left.L_xL_yL_z\Theta\right]-4\int_0^\Theta\int_0^{L_x}\int_0^{L_y}\int_0^{L_z}A_2(x,y,z,t)C(x,y,z,t)R_2(x,y,z,t)N_1^3(x,y,z,t)\,d\,z\,d\,y\,d\,x\times\\
&(\Theta-t)\,d\,t+\int_0^\Theta\int_0^{L_x}\int_0^{L_y}\int_0^{L_z}A_2(x,y,z,t)R_2(x,y,z,t)N_1^4(x,y,z,t)\,d\,z\,d\,y\,d\,x\left[L_xL_yL_z\Theta+\right.\\
&\left.\int_0^\Theta(\Theta-t)\int_0^{L_x}\int_0^{L_y}\int_0^{L_z}M(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t\right]-\int_0^\Theta\int_0^{L_x}\int_0^{L_y}\int_0^{L_z}A_2(x,y,z,t)C(x,y,z,t)\,d\,z\,d\,y\,d\,x+\\
&2\left[\int_0^\Theta(\Theta-t)\int_0^{L_x}\int_0^{L_y}\int_0^{L_z}M(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t+L_xL_yL_z\Theta\right]\int_0^\Theta(\Theta-t)\int_0^{L_x}\int_0^{L_y}\int_0^{L_z}A_2(x,y,z,t)\times\\
&N_1(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t-3\int_0^\Theta\int_0^{L_x}\int_0^{L_y}\int_0^{L_z}A_2(x,y,z,t)\,N_1(x,y,z,t)R_1(x,y,z,t)\,d\,z\,d\,y\,d\,x\times\\
&(\Theta-t)\,d\,t-\int_0^\Theta(\Theta-t)\int_0^{L_x}\int_0^{L_y}\int_0^{L_z}C(x,y,z,t)R_2(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t+3\int_0^\Theta(\Theta-t)\times\\
&\int_0^{L_x}\int_0^{L_y}\int_0^{L_z}R_2(x,y,z,t)N_1(x,y,z,t)A_1(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t+2\int_0^\Theta\int_0^{L_x}\int_0^{L_y}\int_0^{L_z}R_2(x,y,z,t)\times\\
&N_1(x,y,z,t)A_1(x,y,z,t)\,d\,z\,d\,y\,d\,x\,(\Theta-t)\,d\,t\left[\int_0^\Theta(\Theta-t)\int_0^{L_x}\int_0^{L_y}\int_0^{L_z}M(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t+\right.\\
&\left.L_xL_yL_z\Theta\right]-6\int_0^\Theta\int_0^{L_x}\int_0^{L_y}\int_0^{L_z}R_2(x,y,z,t)N_1^2(x,y,z,t)A_2(x,y,z,t)C(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t\times\\
&(\Theta-t)\,d\,t+4\int_0^\Theta(\Theta-t)\int_0^{L_x}\int_0^{L_y}\int_0^{L_z}R_2(x,y,z,t)N_1^3(x,y,z,t)A_2(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t\times\\
&\left[\int_0^\Theta(\Theta-t)\int_0^{L_x}\int_0^{L_y}\int_0^{L_z}M(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t+L_xL_yL_z\Theta\right]-\int_0^\Theta(\Theta-t)\int_0^{L_x}\int_0^{L_y}\int_0^{L_z}A_2(x,y,z,t)\times\\
&R_1(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t+\int_0^\Theta(\Theta-t)\int_0^{L_x}\int_0^{L_y}\int_0^{L_z}A_2(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t\left[L_xL_yL_z\Theta+\right.\\
&\left.\int_0^\Theta(\Theta-t)\int_0^{L_x}\int_0^{L_y}\int_0^{L_z}M(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t\right]+\int_0^\Theta\int_0^{L_x}\int_0^{L_y}\int_0^{L_z}A_1(x,y,z,t)R_2(x,y,z,t)\,d\,z\,d\,y\,d\,x\times\\
&\times(\Theta-t)\,d\,t+\left[\int_0^\Theta(\Theta-t)\int_0^{L_x}\int_0^{L_y}\int_0^{L_z}M(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t+L_xL_yL_z\Theta\right]\int_0^\Theta(\Theta-t)\times
\end{aligned}
$$

$$\int_0^{L_x}\int_0^{L_y}\int_0^{L_z} R_2(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t - \int_0^{\Theta}(\Theta-t)\int_0^{L_x}\int_0^{L_y}\int_0^{L_z} A_2(x,y,z,t)R_2(x,y,z,t)\,C(x,y,z,t)\times$$
$$4\left[N_1(x,y,z,t)+1\right]d\,z\,d\,y\,d\,x\,d\,t + 6\left[\int_0^{\Theta}(\Theta-t)\int_0^{L_x}\int_0^{L_y}\int_0^{L_z} M(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t + L_xL_y\times\right.$$
$$\left.L_z\Theta\right]\int_0^{\Theta}(\Theta-t)\int_0^{L_x}\int_0^{L_y}\int_0^{L_z} A_2(x,y,z,t)R_2(x,y,z,t)\,N_1^2(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t + 4\int_0^{\Theta}(\Theta-t)\times$$
$$\int_0^{L_x}\int_0^{L_y}\int_0^{L_z} A_2(x,y,z,t)R_2(x,y,z,t)\left[N_1(x,y,z,t)+1\right]d\,z\,d\,y\,d\,x\,d\,t\left[L_xL_yL_z\Theta+\right.$$
$$\left.\int_0^{\Theta}(\Theta-t)\int_0^{L_x}\int_0^{L_y}\int_0^{L_z} M(x,y,z,t)\,d\,z\,d\,y\,d\,x\,d\,t\right]. \qquad (11)$$

The spatial-temporal distribution of the quantity of tumor cells was analyzed analytically by using the second-order approximation in the framework of the method of averaging function corrections. The approximation is usually a good enough approximation to make a qualitative analysis and obtain some quantitative results. All the obtained results have been checked by comparison with the results of numerical simulations.

DISCUSSION

In this section, we analyzed the changes in the distribution of the quantity of tumor cells in an organism over space and time. Figure 1 shows typical dependences of the considered quantity on coordinates at constant values of parameters. Depending on the values of the parameters in equation (1), the tumor may grow or shrink. The rate of change in the size of the tumor could also be changed. The effectiveness of the chemotherapy drug increases when combined with an external low-intensity physical factor that increases the biological activity of both tumor cells and tumor tissue. External physical factors become with their spatial inhomogeneity. Decreasing of size of the neoplasm during treatment in the framework of the considered was observed when the intensity of the external field is above a certain threshold level. The similar conclusion was qualitatively obtained in the following references [12,13].

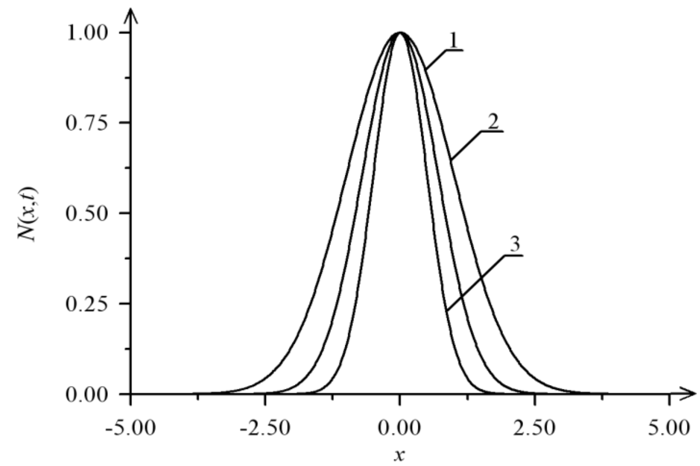

Fig. 1. Typical normalized dependences of quantity of tumor cells on co-ordinate

CONCLUSION

We introduced a model for the description of the development of tumors. The model gives the possibility to take into account the development of the tumor's own cells, the effects of chemotherapeutic drugs on them, as well as their interaction with surrounding cells. We also introduced an analytical approach for the analysis of the considered model. The approach gives the possibility of taking into account changes in the conditions of the considered processes. We also consider the possibility of changing their rates.

REFERENCES

[1] Kashevsky, B.E., Ulashchik, V.S., Yu.P. Istomin, Kashevsky, S.B., Prokhorov, I.V., Pastushenko, A.G, 2010.Reports of the National Academy of Sciences of Belarus. 54 (2) 114-7.
[2] Naumenko, V.Yu., Akopdzhanov, A.G., Babich, A.V., Bykov, I.V., Shimanovsky. N.L., 2011.Biomedical radio electronics. I12,19-27.
[3] Klepper. L.Ya. 2015. Medical physics. 2.23-33.
[4] Stolbovoy, A.V., Zavyalov. I.F.,2016. Radiobiological models and clinical radiation oncology. 6, 88-96.
[5] Ternovoy, S.K. Fundamentals of radiation diagnostics and therapy. National leadership (Moscow, GEOTAP-Mediab, 2012).
[6] Vasin, M.V, 2013. Radiation biology. Radioecology. 53 (5) 459-467.
[7] Guiliano, N.Y., Noskin, L.A., Zhurishkina, E.V., Stepanov, S.I., Ibatullin, F.M., Torshin, V.I., Yakunina, E.B., Alchinova. I.B.,2019. Pathological physiology and experimental therapy. 63 (2) 41-49.
[8] Yu.D. Sokolov.1955. Applied mechanics. 1 (1)23-35.
[9] Pankratov, E.L Bulaeva. E.A.2014. International Journal of Modern Physics B. 28 (27) 1450190-1-1450190-17
[10] Pankratov, E.L., Bulaeva. E.A. 2015.Reviews in Theoretical Science. 3 (4) 365-398.
[11] Pankratov, E.L. 2023. Int. J. Adv. Sci. Eng. 9 (4) 3047-3071.
[12] Orel V.E., Nikolov M.O., Dzyatkovska N.M. 2008. Physics of the living. 16 (2) 92-98.
[13] Karpenko V.I., Korostinska O.S., Loshitskiy P.P., Nikolov M.O. 2000. Biology and ecology. 18 51-55.